ASHG 2006 Award for Excellence in Genetics Education

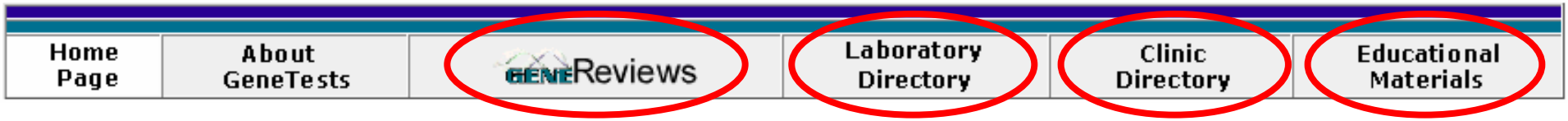
Roberta A. Pagon, MD
Principal Investigator, GeneTests
Professor, Pediatrics
University of Washington, Seattle

www.genetests.org

Information resource for healthcare providers to help integrate genetic services into patient care

Located at
University of Washington
Seattle, WA

Funded by
National Institutes of Health

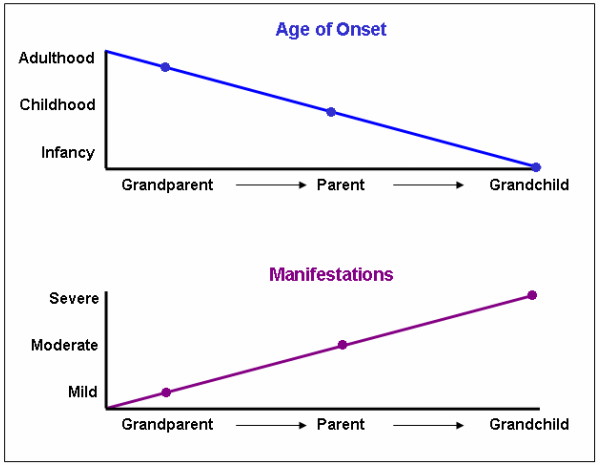


- ***GeneReviews*:** "User manual" for genetic testing for specific diseases
  - 360 *GeneReviews*
  - One new Review added each week
- **Laboratory Directory:** "Yellow Pages" of genetics labs
  - 600 Clinical and research laboratories
  - ~1225 Inherited diseases
  - ~930 clinical tests ~295 research only
- **Clinic Directory:** "Yellow Pages" of genetic services
  - 1100 clinics
- **Illustrated Glossary:** Genetic counseling and testing terms

- **Illustrated Glossary:** Genetic counseling and testing terms

Learn More

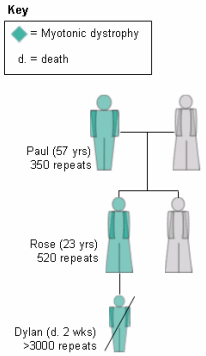
anticipation: The tendency in certain genetic disorders for individuals in successive generations to present at an earlier age and/or with more severe manifestations; often observed in disorders resulting from the expression of a **trinucleotide repeat mutation** that tends to increase in size and have a more significant effect when passed from one generation to the next



Case Example

Case Example (anticipation): Myotonic dystrophy

Paul is a 57-year-old man with myotonic dystrophy, a neuromuscular disorder caused by a trinucleotide repeat mutation inherited in an autosomal dominant manner. Paul noticed muscle weakness in his late 20s and now has difficulty opening jars and climbing stairs. His 23-year-old daughter, Rose, experienced onset of muscle cramping and weakness as a teenager. Her son, Dylan, born after a pregnancy complicated by polyhydramnios and poor fetal movement, was extremely hypotonic and expired at two weeks of age of respiratory failure. Trinucleotide repeat analysis of the *DMPK* gene reveals that Paul has 350 CTG repeats, Rose has 520 repeats and Dylan over 3000 repeats, consistent with the observed increase in severity of the disorder in subsequent generations.



	DMPK gene CTG Repeats	Onset	Clinical Findings
Paul	350	3rd decade	Myotonia, weak facial muscles, general muscle weakness
Rose	520	2nd decade	Myotonia, weak facial muscles, general muscle weakness
Dylan	>3000	Prenatal	Severe weakness, respiratory failure

GENETests

Molecular genetic testing for inherited disorders

- **Test menu ever-changing**
  - New genes
  - New test methods
- **Many labs, each testing for a few diseases**
- **Molecular genetic test uses**
  - Medical care: Diagnosis, predictive testing (+Rx)
  - Personal decision-making: Predictive testing (-Rx), carrier testing, prenatal diagnosis, PGD

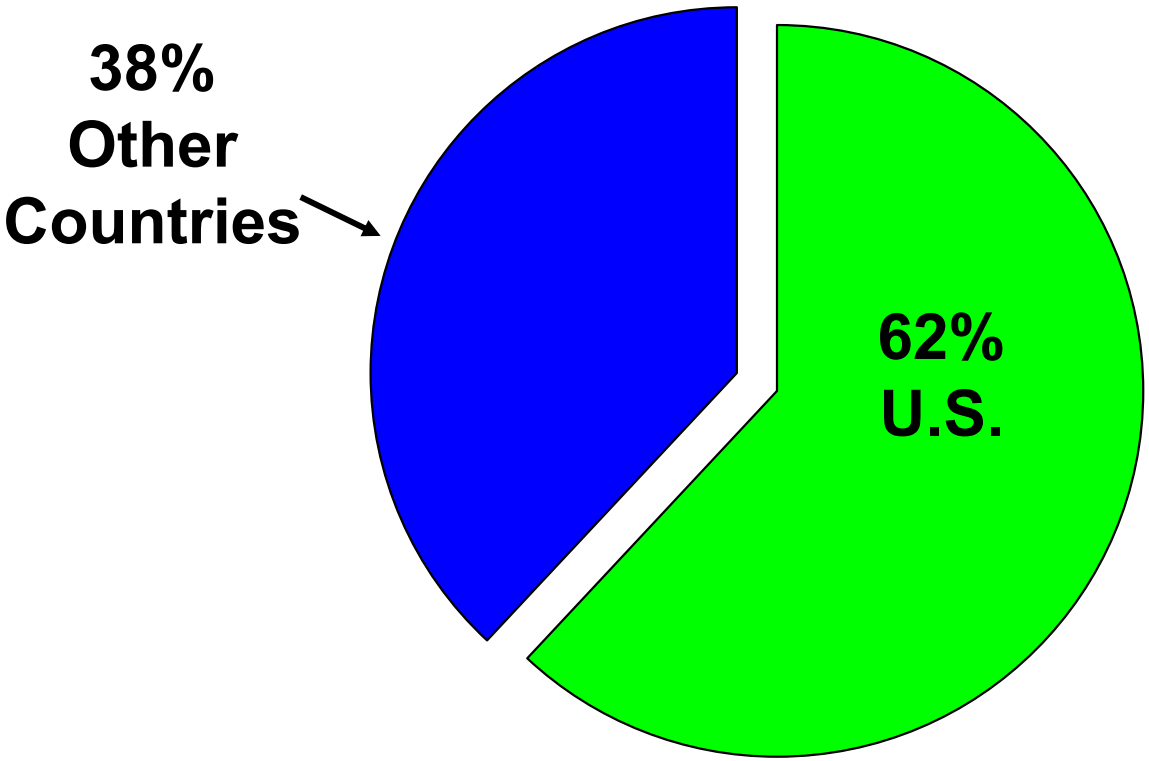
GENETests

Integrating genetic services into patient care

- **Acknowledgments**
- Education issues
- Help us improve GeneTests

GENEReviews

~800 International Expert Authors



GENETests

GENEReviews

Authors

- **No financial compensation**
- **Must**
  - Adhere to *GeneReviews* format, style
  - Respond to internal and external peer review
- **Two year term of authorship**
  - Revise when test availability/methods change
  - Update every two years

GENEReviews

Reviewers

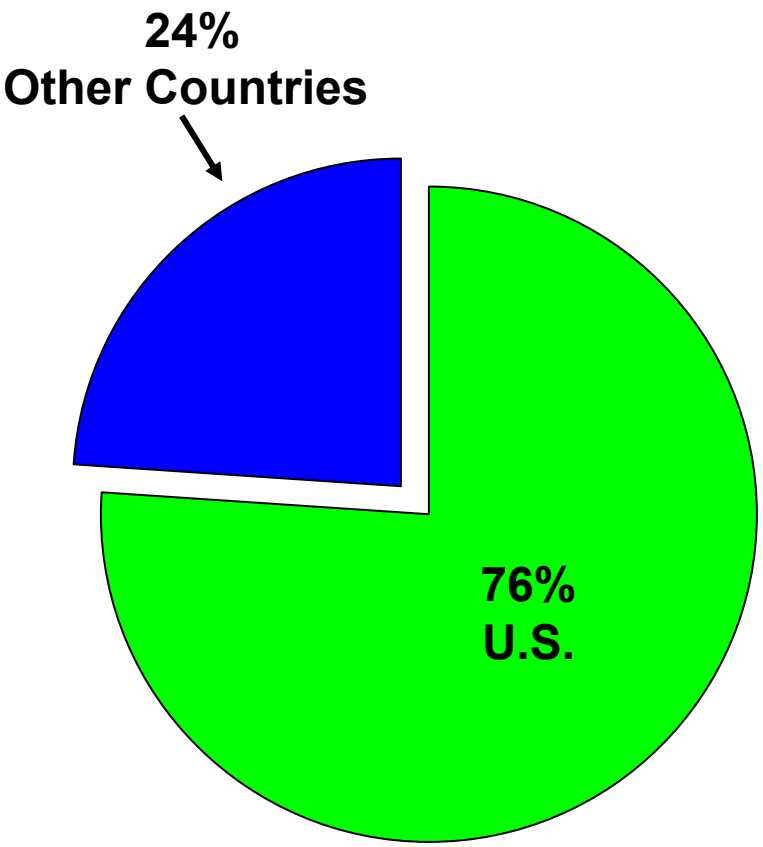
- **No financial compensation**
- **Review for:**
    - Accuracy
    - Currency
    - Suitability for healthcare providers

GENETests

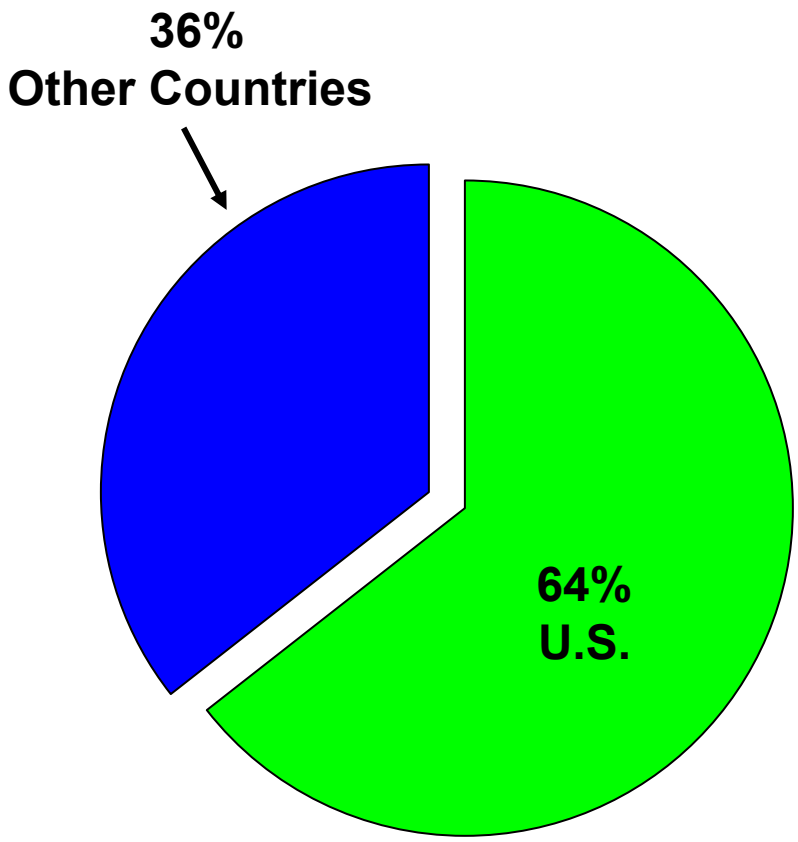
GENETests

Laboratories

2001 (N = 498)



2006 (N = 642)



GENETests

Clinics

Countries with clinics listed with GeneTests

Argentina
Australia
Austria
Bahrain
Belgium
Brazil
Canada
Chile
Czech Republic
Denmark
Egypt
France
Germany
India
Israel
Italy
Japan
New Zealand
Norway
Portugal
Russia
South Korea
Spain
United Kingdom
United States

GENETests

Integrating genetic services into patient care

- Acknowledgments
- **Education issues**
- Help us improve GeneTests

Education Issues

Vocabulary

- Geneticists talk “funny”
- Do we really know what we are saying?

Vocabulary: What are we saying?

Sporadic vs Simplex:
Recurrence risk implications

- Sporadic = Chance event
- Simplex = Single occurrence in a family
  - Autosomal recessive
  - X-linked
  - Autosomal dominant: *de novo* mutation, reduced penetrance
  - Alternate paternity/adoption

Education Issues

Disease naming

- Gene-based lumping and splitting of phenotypes

- What disease is this?

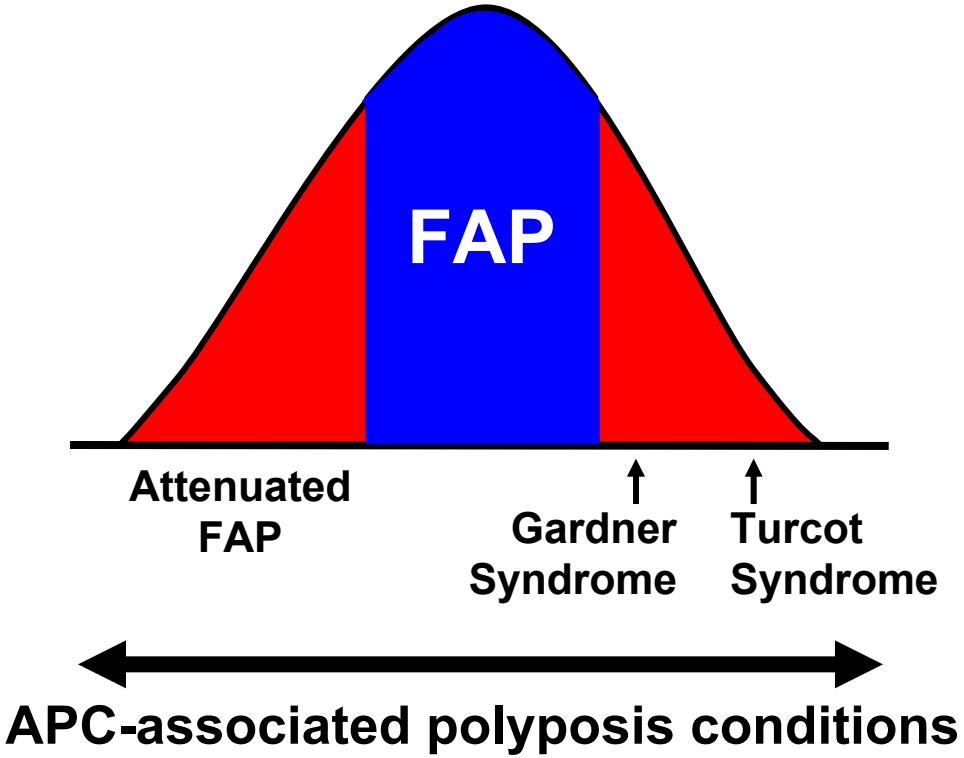
Disease naming: What disease is this?

- **Laboratory:** Testing detects alterations in a gene, not a phenotype
- **Clinician:** Patients present with altered phenotypes
- **Disease name**: Relate to genes for laboratories; relate to phenotypes for clinicians

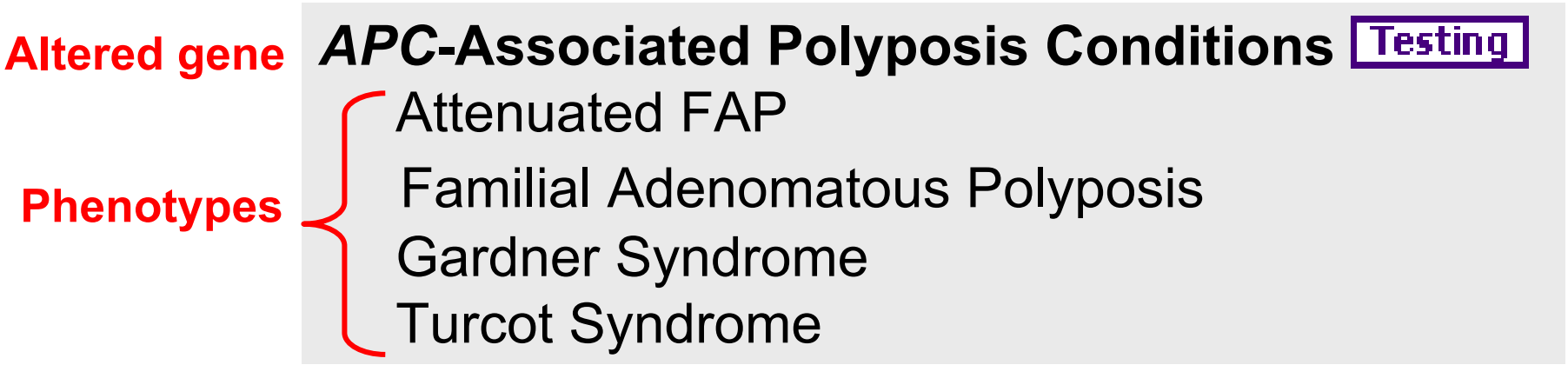
Disease Naming

1. Pre-gene discovery: Phenotype is narrowly defined – Essential to gene discovery

2. Post-gene discovery: Phenotypic spectrum expands as patients are tested – Essential to patient care



Naming Hierarchy



Naming Hierarchy

Altered gene ***FMR1*-related disorders** Testing

Phenotypes

- Fragile X syndrome
- FMR1-related premature ovarian failure
- Fragile X-associated tremor/ataxia syndrome

GENETests

Incorporating genetic services into patient care

- Acknowledgments
- Education issues
- **Help us…**

GENETests

Staff: Laboratory and Clinic Directories

Gina McCullough Grohs
Laboratory Directory
Coordinator

Roberta Spiro, MS, CGC
Genetic Counselor
Clinic Directory
Coordinator

Kathi Marymee, MS, CGC
Resources Liaison

GENETests

Staff: *GeneReviews* Editorial Staff

Cynthia R Dolan, MS, CGC
Associate Editor

Suzanne B Cassidy, MD
Assistant Editor

Thomas D Bird, MD
Associate Editor

Mary Beth P Dinulos, MD
Assistant Editor

Gerald L Feldman, MD, PhD
Associate Editor

GENETests

Staff: *GeneReviews* Production Team

Monica Smersh
Managing Editor

Miriam Espeseth, MA
Online Production Editor

Cindy Abair, MA
Graphics Editor

Carla Gifford
Editorial Assistant

GENETests

Staff: Information Technology

Sergey Mikhaylov, MS
Database Administrator

Brad Willson
Systems Administrator

Help us… improve GeneTests

Contact us:

- Errors
- Ideas to improve the site
- Potential collaborations

Refer:

- Labs/clinics
- New users

Volunteer: Write a *GeneReview*

Assign students: Projects????

GENETests

Thank you for this honor